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<b>(21) International Application Number:</b> PCT/AU99/00607 <b>(22) International Filing Date:</b> 28 July 1999 (28.07.99) <b>(30) Priority Data:</b> PP 4897 28 July 1998 (28.07.98) AU <b>(71) Applicant (for all designated States except US):</b> MEDIKO PTY. LTD. [AU/AU]; 59A Armadale Street, Armadale, VIC 3143 (AU). <b>(72) Inventor; and</b> <b>(75) Inventor/Applicant (for US only):</b> KO, Thomas, Sai, Ying [AU/AU]; 4 Licence Road, Belgrave South, VIC 3160 (AU). <b>(74) Agents:</b> STEARNE, Peter et al.; Davies Collison Cave, Level 10, 10 Barrack Street, Sydney, NSW 2001 (AU).			<b>(81) Designated States:</b> AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report.</i>
<b>(54) Title:</b> HAIR GROWTH/MAINTENANCE COMPOSITIONS AND METHODS INVOLVING THE SAME			
<b>(57) Abstract</b>  Hair growth/maintenance compositions are disclosed which include water, a water soluble film forming polymer, and an immune modulatory compound in an amount effective to promote hair growth/maintenance. Also disclosed are methods for hair growth/maintenance and uses directed to hair growth/maintenance.			
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## HAIR GROWTH / MAINTENANCE COMPOSITIONS AND METHODS INVOLVING THE SAME

### 5 Field of the Invention

This invention relates to hair growth/maintenance compositions and methods for hair growth/maintenance. More particularly the invention is concerned with compositions for application to the scalp which prevent hair loss, and provide for new hair growth.

### 10 Background of the Invention

Hair loss, thinning of hair and baldness have been a fact of human life which affects countless people worldwide, both male and female. These conditions often cause self-consciousness and acute embarrassment to the sufferer. Lack of confidence and psychological disturbance can sometimes result.

15

People have gone to great lengths to treat hair loss, thinning hair and baldness, as is evidenced by the myriad approaches used to deal with these problems. Non-surgical approaches appear to be largely ineffective. Insofar as surgical approaches are concerned, procedures such as implanting hair follicles taken from other portions of the body into the  
20 scalp are expensive, inconvenient and sometimes painful procedures. Generally, other surgical approaches also suffer these disadvantages.

Hair pieces or toupees are often used by people whose hair is thinning, and by those who have bald patches. These devices may be regarded as uncomfortable to wear, and highly  
25 embarrassing if dislodged during wear. Such devices may be expensive and often have a unnatural appearance which may not reflect the other hair colour of the wearer. This is particularly evident when the natural hair lightens, turning gray or white with age.

Compositions directed to women suffering from hair loss resulting from factors such as  
30 hormonal changes or disturbances, age or the like, are generally in the form of hair firming gels. These products appear to attract dirt from the air, requiring frequent washing of the hair. These compositions may also irritate the scalp in some people.

US Patent No. 4,737,362 ("Yoshizumi") describes hair treatment compositions purported  
35 to accelerate hair growth which contain bacterial derived lipase, a lipid degrading enzyme which appears to have an antibacterial activity. Such compositions have the disadvantages of causing hair dryness, scalp itchiness and irritation, an unpleasant odor after application to the skin, and possible skin/scalp damage with prolonged use.

The present invention addresses the problems of the prior art detailed above and provides a simple, cost effective and convenient solution to hair growth/maintenance.

- 5 The inventor has surprisingly found that compositions containing immune modulatory compounds, namely compounds known to modulate the immune system, are particularly suitable in stimulating new hair growth and/or maintaining hair growth (preventing hair loss). The compounds are applied to the hair in a formulation containing water and a water soluble film forming polymer.

10

### Summary of the Invention

In accordance with a first aspect of this invention there is provided a hair growth/maintenance composition which includes water, a water soluble film forming polymer and an immune modulatory compound in an amount effective to promote hair  
15 growth/maintenance.

In another aspect of the invention, there is provided a method for hair growth/maintenance which includes applying to the scalp, or other areas of skin, a composition comprising water, a water soluble film forming polymer, and an immune modulatory compound in an  
20 amount effective to promote hair growth/maintenance.

In a still further aspect of the invention there is provided use of compounds known to modulate the immune system in combination with a film forming polymer and water in the manufacture of a medicament for the treatment of baldness and hair maintenance.

25

### Brief Description of the Drawings

In the figures, Figures 1 to 10 depict the scalp of individuals treated with the compositions of the examples, at the beginning of treatment and after treatment.

- 30 Fig 1: Top view of the scalp of a 45 year old man prior to treatment (A), and scalp after 3 months treatment (B).

Fig 2: Top view of the scalp of a 67 year old male showing a pronounced bald patch prior to treatment.

35

Fig 3: View from above of side and top of scalp of Fig 2 subject after 3 months treatment.

Fig 4: View of top of scalp of volunteer 001 before (A) and after 10 months treatment (B).

Fig 5: View of rear of scalp of volunteer 002 before treatment (A), after 3 months treatment (B) and after 6 months treatment (C).

Fig 6: Top view of the scalp of volunteer 004 before treatment (A) and after 3 months treatment (B).

Fig 7: Top view of the scalp of volunteer 006 before treatment (A) and after 3 months treatment (B).

Fig 8: Top view of the scalp of volunteer 008 before treatment (A) and following 3 months treatment (B).

Fig 9: Top view of the scalp of volunteer 009 before treatment (A) and after 3 months treatment (B).

### Detailed Description of the Invention

This invention relates to compositions which provide new hair growth, and prevent hair loss. Compositions which are conveniently applied to the scalp allow for ready treatment of hair loss, thinning hair and baldness. In a first aspect the invention provides a hair growth/maintenance composition which includes water, a water soluble film forming polymer, and an immune modulatory compound in an amount effective to promote hair growth/maintenance.

A hair growth/maintenance composition in accordance with this invention represents a significant advance in the treatment of hair loss, thinning hair and baldness. On application to the scalp, the composition forms a thin film over hair, hair follicles and scalp allowing maximum effectiveness. By hair growth is meant new hair growth. Hair maintenance means that hair follicles continue to produce hair rather than regress and die.

The water soluble film forming polymer may be selected from one or more natural or synthetic water soluble film forming polymers such as acacia, albumins, agar, alginic acid and its salts, bentonites, carbomer, carrageenan, carboxy methyl cellulose and its salts, salts of cellulose acetate phthalate, cyclodextrins, dextran, dextrans, gelatin, hydroxy ethyl

cellulose, hydroxy propyl cellulose, hydroxy propyl methyl cellulose, hydroxy propyl methyl cellulose phthalate, and other cellulose derivatives, ispaghula, lecithins, lanoline alcohols, maltodextrins, pectin, povidone, polyvinyl povidone, poly vinyl acetate, starches, tragacanth, and the like. The precise nature of the film forming polymer is  
5 generally unimportant, as long as it forms a convenient thin film on application to the scalp.

Once the composition dries on the scalp, the composition is unnoticeable. Where hair is present on the scalp, the hair is imparted with greater body to give a more full appearance,  
10 which is also pleasing to the eye.

The immune modulatory compound is a compound which modulates the immune response, for example attenuating, facilitating or stimulating some aspect of the immune response, whether humoral or cellular, preferably immune stimulating compounds, such as  
15 muramidase (otherwise known as lysozyme hydrochloride or globulin G1), interferons such as interferon  $\alpha$ ,  $\beta$  and  $\gamma$ , non-inflammatory interleukins, insulin-like growth factor-1 (IGF-1), epidermal growth factor (EGF), extract of Echinacea, mannin, heteroxylan, arabinorhamnogalactan,  $\beta$ -glucan, and other compounds having immune stimulatory function. Muramidase is particularly preferred. Immune modulatory compounds do not  
20 induce cell transformation/immortalisation (as may occur with fibroblast growth factor, TFG-13, keratinocyte growth factor, and the like) which may result in cancerous states. Interleukin  $1\alpha$ , interleukin  $1\beta$ , TNF- $\alpha$ , and TNF- $\beta$  are specifically excluded as these proteins have been found to inhibit hair growth. The compositions of this invention may include two or more immune modulatory compounds.

25

The compositions of the present invention generally include from 0.01% to 10% (w/w) immune modulatory compound, preferably 0.05% to 1% (w/w) - where the immune modulatory compound is muramidase it is generally present in an amount from about 0.01% to about 10% (w/w), preferably about 0.05% to about 1% (w/w). Where the  
30 immune modulatory compound is an interferon it is generally present in an amount from about 1IU to about 10,000IU. Where the immune modulatory compound is  $\beta$ -glucan it is generally present in an amount from about .01mg to about 200mg/ml, preferably about, preferably about 0.1mg to about 50mg/ml. Where the immune modulatory compound is a non-inflammatory interleukin (as can be readily determined in experimental animals), such  
35 as interleukin  $1\beta$ (163-171) the compound is generally present in an amount from 0.01mg to 100mg/ml, preferably 0.1mg to 20mg/ml.

The immune modulatory compounds may be in the form of any pharmaceutically acceptable salts as are known in the art, such as hydrochloride and phosphate salts.

The water soluble film forming polymer is generally present in an amount of about 0.01 %  
5 to 10% (w/w), preferably 0.05 % to 5% (w/w), and more preferably 0.1 % to 1 % (w/w).

The composition of the invention may include conventional carriers, excipients, buffers, preservatives and wetting agents used in compositions for the application to the skin or scalp, such as ethylene diamine tetra acetic acid (EDTA), dextran, sodium acid phosphate,  
10 disodium phosphohate, potassium acid phosphate, dipotassium phosphate, sodium benzoate, propyl hydroxy benzoate, methyl hydroxy benzoate, buffering compounds, salts, detergents (such as sodium lauryl sulphate, and sodium dodecylsulphate) and emulsifiers, and the like. Such components may be present in amounts from about 0.01 % (w/w) to about 10% (w/w). By way of example, detergents may be present in an amount from  
15 about 0.01 % (w/w) to about 5 % (w/w).

The compositions of the present invention may be applied to the scalp by way of direct application, such as pouring a small amount of the composition on to the scalp or on to the fingers, and then rubbing this material over the scalp or affected areas. Alternatively, the  
20 composition may be sprayed using conventional spraying apparatus such as an air-driven spray arrangement, or misting arrangement, as are widely used in the application of perfumes and cosmetics formulations.

Compounds which assist in stabilizing the immune modulatory compound may be included  
25 in the composition, such as trehalose, a sugar well known for such a purpose.

Water constitutes the balance of the composition of the invention, the result being a solution of dissolved components in water which can be readily applied to the scalp by conventional means.

30

The compositions of the present invention preferably do not contain any chemical propellant, alcohol, artificial colourings, or chemicals which may cause scalp irritation. However, one or more such components may be present in amounts which do not cause scalp irritation.

35

The composition of the invention may be applied daily or at least once every three days. Generally, such use prevents hair loss within four weeks. Visible difference in hair

recovery, that is new hair growth, is generally observed over a two to twelve month period of continued use. Continued use of the product on a daily basis, or once every three days, prevents hair loss and actively promotes hair growth.

- 5 Subjects which may be treated according to this invention are human males and females who are subject to hair loss, hair thinning, and/or baldness. Animals suffering from such conditions may also be treated with the compositions of this invention.

In another aspect the invention provides a method for hair growth/maintenance which  
10 comprises applying to the scalp, or other areas of skin, a composition comprising water, a water soluble film forming polymer, and an immune modulatory compound in an amount effective to promote hair growth/maintenance.

In a method according to an aspect of this invention, a composition as described above is  
15 applied to the scalp or area of skin to which it is desired that hair growth/maintenance takes place. Application is preferably made to the scalp/skin on a once daily basis. The composition may be sprayed or poured on to the area to be treated and may be gently rubbed in with the fingers or conveniently brushed or combed through the hair and scalp. The composition forms a thin and unnoticeable film on the scalp or skin, and a thin  
20 unnoticeable film on any hair present. The composition imparts body or fullness to whatever hair remains which improves the appearance of the person being treated, and additionally prevents hair loss and promotes hair growth.

As mentioned above, hair loss is generally prevented within four weeks of treatment and a  
25 visible difference in hair recovery is observed generally within two to twelve months of continued use of the composition according to the invention.

The precise mechanism of action of the composition/method of the invention is unclear. Without wishing to be bound by any theory of action, the inventor believes that immune  
30 modulatory compounds may modulate the immune response at the level of the hair follicle, in cooperation with the film forming polymer, in a manner which prevents hair loss and stimulates new hair growth. The compositions of this invention may reverse an abnormal cycle associated with hair loss/baldness by extending the growth phase of hair follicles and reducing the regressional phase, which may explain the slowing/prevention of the  
35 balding/hair loss process and new hair growth in a natural manner.



This invention will now be described with reference to the following non-limiting Examples.

### Example 1

5

The following formulation was prepared:

Muramidase	100 mg
Gelatin	100 mg
Trehalose	100 mg
EDTA di sodium	140 mg
Dextran	250 mg
Sodium acid phosphate	270 mg
Sodium phosphate	1160 mg
Propyl hydroxy benzoate	30 mg
Methyl hydroxy benzoate	90 mg
Purified water	100 ml

10 Other formulations were made where lysozyme was replaced with interferon- $\alpha$ , interferon- $\beta$ , interferon- $\gamma$ , interleukin-1 $\beta$ (163-171) peptide, insulin-like growth factor-1 (IGF)-1, epidermal growth factor (EGF), extract of Echinacea, mannin, heteroxylan, arabinorhamnogalactan, and  $\beta$ -glucan and non-inflammatory interleukins. All of these immune modulatory compounds are widely available from pharmaceutical/chemical  
15 suppliers.

### Example 2

Mrs K, a mature woman, began to loose a significant amount of hair each day and developed a visible receding hairline on the left side of her head, noticeable from the front  
20 of the scalp. To ameliorate this problem, Mrs K had used a non-alcohol pre-spray on gel to hold her hair in place to cover up the receding patch. This product attracted dirt from the air and rendered the hair unattractive to the eye. Frequent washing of the hair was required and this may have contributed to continued hair loss. A lysozyme containing composition, according to Example 1, was prepared and sprayed daily on to the affected  
25 area until the hair was slightly wet. Using either a comb, brush, or simply the hand, the slightly moist hair was used to form a shade over the receding area. After three weeks,

Mrs K noticed that hair loss was dramatically reduced, and that there was a proliferation of short hair growth on the affected area.

### Example 3

5 Mr J, a mature man, has a receding hair line from both sides of the scalp and was loosing hair on a daily basis, which had become quite visible. Mr J began applying the muramidase composition according to Example 1 to the affected area on a daily basis. As a control, a small amount of the composition was sprayed on to the right elbow using the left side of the elbow as a control. Patch tests were also carried out where the composition  
10 was sprayed on both wrists, where Mr J had very fine short hairs, such that any growth was visible and able to be monitored. In this test, the composition was rubbed on to the surface of the skin for ten seconds at one finger width across each wrist. After two months there was a noticeable hair growth on the balding patch of the scalp and also hair growing visibly long and thick on the test patches with no additional hair growth on the  
15 control sites.

After twelve months of use on a daily basis of the muramidase containing composition, Mrs K and Mr J no longer have a receding hair problem, and their hair has visibly grown back.

20

### Example 4

The composition containing muramidase has been tested on approximately one hundred people, suffering from various stages of thinning hair, hair loss and baldness. The majority of test subjects have found that hair loss has been prevented after about four  
25 weeks of use and that new hair growth is observed.

It has also been observed that the hair growth is generally the original colour of the hair of the person. If the user of the composition is already white/gray hair, the new hair growth is not generally white/gray hair but the original hair colour of the person prior to the hair  
30 turning white/gray.

Figure 1 shows the photograph of a scalp of a forty five year old user who had been bald for more than fifteen years. Following daily application of the composition, according to Example 1, hair follicle and new hair growth is visible only after two months of use, as is  
35 evident in Figure 2.

Figure 3 shows a photograph the scalp of a sixty seven year old male, with a bald patch among white hair with very little side growth. After application of the composition, according to example 1, for three months the new growth of black hair can be seen in figure 4, which hair was not present before treatment.

5

Results of a pilot study on 6 individuals who applied the composition according to Example 1 containing muramidase to their scalp on a daily basis is set out below.

Volunteer No.	Gender	Age	Baldness history	Time in Treatment	Comments
001	M	35	10 years	14 months	Dense fine hair covering the whole crown
002	M	46	20 years	12 months	Most improvement at vertex region, being site of baldness
004	M	32	4 years	9 months	Stopped hair thinning
006	M	26	7 years	8 months	General increase in hair density
008	M	57	5 years	8 months	General increase in density with most improvement at vertex region
009	M	45	20 years	6 months	General increase in hair density

10

Results obtained are shown in Figures 4-9, relating to volunteers 001 to 009 respectively after 3 months treatment. What these figures show is that after 3 months treatment hair loss has not occurred, and new hair growth has been established. Control subjects treated with a composition which did not include muramidase and a film forming polymer

15 (controls) were not effective.

In another set of experiments, compositions according to Example 1 but containing interferon- $\alpha$ , interferon- $\beta$ , interferon- $\gamma$ , interleukin-1 $\beta$ (163-171) peptide or other non-inflammatory interleukins, insulin-like growth factor-1 (IGF-1), extract of Echinacea,

mannin, heteroxylan, arabinorhamnogalactan, or  $\beta$ -glucan in place of muramidase were tested. In the treated subjects new hair growth and prevention of hair loss was observed which was quite satisfactory. However in comparison the results achieved with muramidase were exceptional.

5

The compositions of the invention prevent hair loss, that is, provide maintenance of hair, and provide new hair growth.

Those skilled in the art will appreciate that the invention described herein is susceptible to  
10 variations and modifications other than those specifically described. It is to be understood that the invention includes all such variations and modifications which fall within its spirit and scope. The invention also includes all of the steps, features, compositions and compounds referred to or indicated in this specification, individually or collectively, and any and all combinations of any two or more of said steps or features.

15

Throughout this specification, unless the context requires otherwise, the word "comprise", or variations such as "comprises" or "comprising" or the term "includes" or variations thereof, will be understood to imply the inclusion of a stated element or integer or group of elements or integers but not the exclusion of any other element or integer or group of  
20 elements or integers. In this regard, in construing the claim scope, an embodiment where one or more features is added to any of claims is to be regarded as within the scope of the invention given that the essential features of the invention as claimed are included in such an embodiment.

## CLAIMS

1. A hair growth/maintenance composition which includes water, a water soluble film forming polymer, and an immune modulatory compound in an amount effective to promote hair growth/maintenance.  
5
2. A composition according to claim 1, where in the immune modulatory compound is selected from muramidase, interferon, a non-inflammatory interleukin, insulin-like growth factor-1 (IGF-1), epidermal growth factor (EGF), extract of Echinacea, mannin, heteroxylan, arabinorhamnogalactan, or  $\beta$ -glucan.  
10
3. A composition according to claim 2, wherein said immune modulatory compound is muramidase, interferon- $\alpha$ , interferon- $\beta$ , interferon- $\gamma$ , interleukin-1 $\beta$ (163-171) peptide, or  $\beta$ -glucan.  
15
4. A composition according to claim 2, wherein said immune modulatory compound is muramidase.
5. A composition according to claim 1 which includes two or more immune modulatory compounds.  
20
6. A composition according to claim 1, wherein said water soluble film forming polymer is selected from natural or synthetic water soluble film forming polymers including acacia, albumins, agar, alginic acid and its salts, bentinites, carbomer, carrageenan, carboxy methyl cellulose and its salts, salts of cellulose acetate phthalate, cyclodextrins, dextran, dextrans, gelatin, hydroxy ethyl cellulose, hydroxy propyl cellulose, hydroxypropyl methyl cellulose, hydroxypropyl methyl cellulose phthalate, and other cellulose derivatives, ispaghula, lecithins, lanoline alcohols, maltodextrins, pectin, povidone, polyvinyl povidone, poly vinyl acetate, starches and tragacanth.  
25  
30
7. A method for hair growth/maintenance which comprises applying to the scalp, or other areas of skin, a composition comprising water, a water soluble film forming polymer, and an immune modulatory compound in an amount effective to promote hair growth/maintenance.  
35
8. A method according to claim 7, where in the immune modulatory compound is selected from muramidase, interferon, a non-inflammatory interleukin, insulin-like

growth factor-1 (IGF-1), epidermal growth factor (EGF), extract of Echinacea; mannin, heteroxylan, arabinorhamnogalactan, or  $\beta$ -glucan.

- 5 9. A method according to claim 7, wherein said immune modulatory compound is interferon- $\alpha$ , interferon- $\beta$ , interferon- $\gamma$ , interleukin-1 $\beta$ (163-171) peptide, or  $\beta$ -glucan.
10. A method according to claim 7, which comprises two or more immune modulatory compounds.
- 10 11. A method according to claim 7, wherein said immune modulatory compound is muramidase.
12. A method according to claim 7, wherein the composition is applied topically to  
15 the scalp on a daily basis or at least once every three days.
13. Use of compounds known to modulate the immune system in combination with a film forming polymer and water in the manufacture of a medicament for the treatment of baldness and hair maintenance.

20

FIG 1

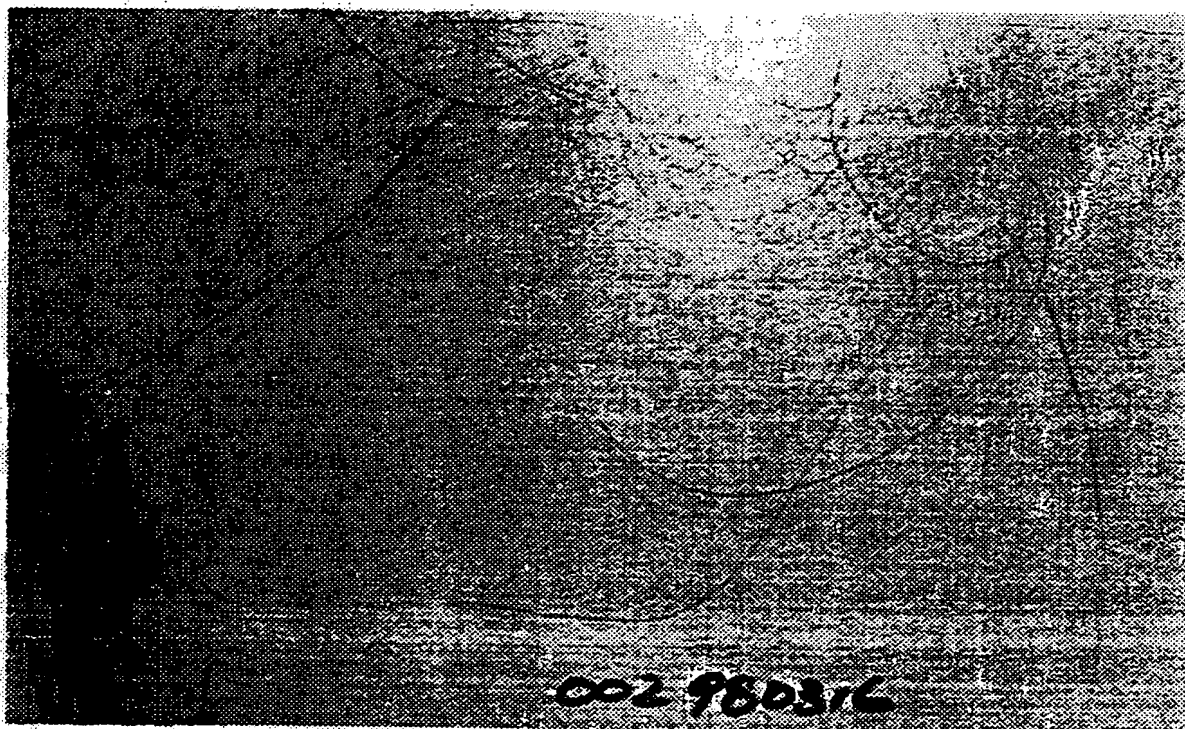
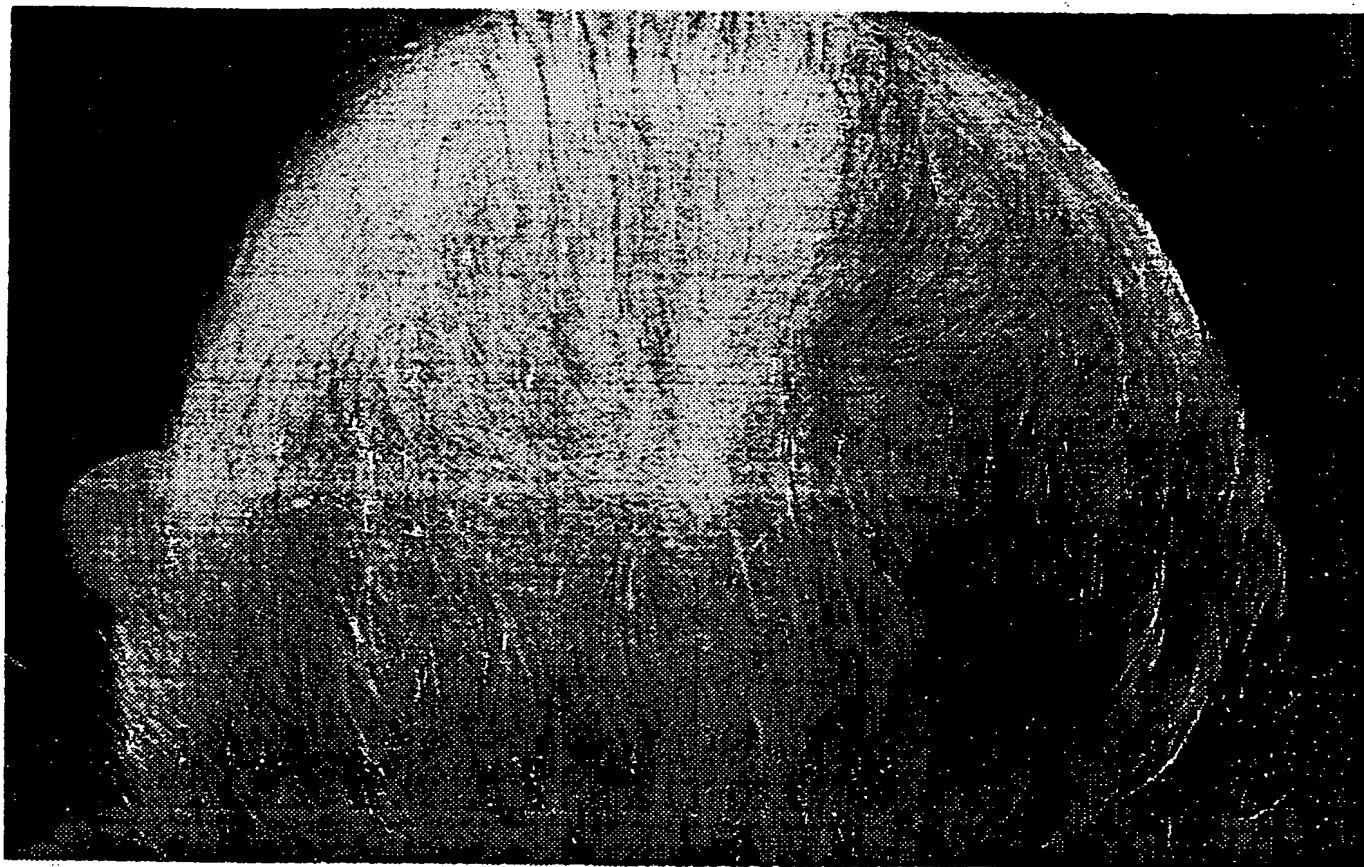


Fig 1A



Fig 1B

FIG 2





3/9

FIG 3



FIG 4

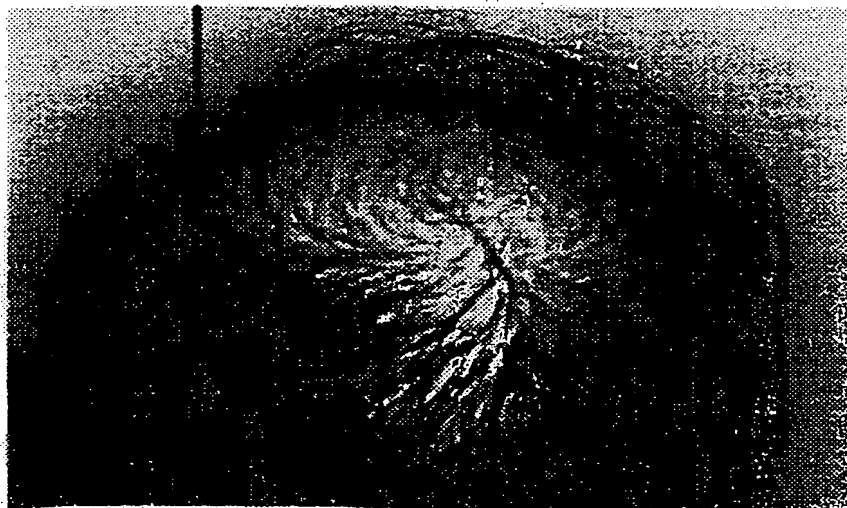


Fig 4A

Fig 4B

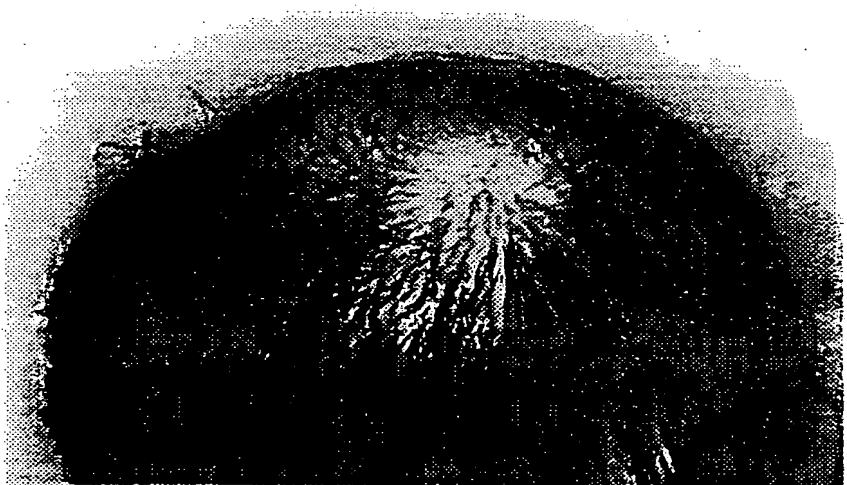
5/9

FIG 5



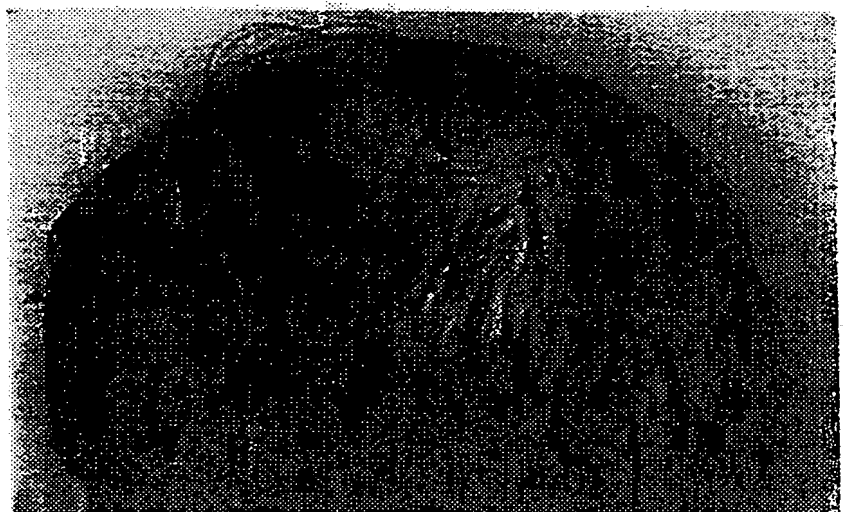
(A)

Fig 5A



(B)

Fig 5B



(C)

Fig 5C

FIG 6



Fig 6A



Fig 6B

FIG 7



Fig 7A



Fig 7B

FIG 8

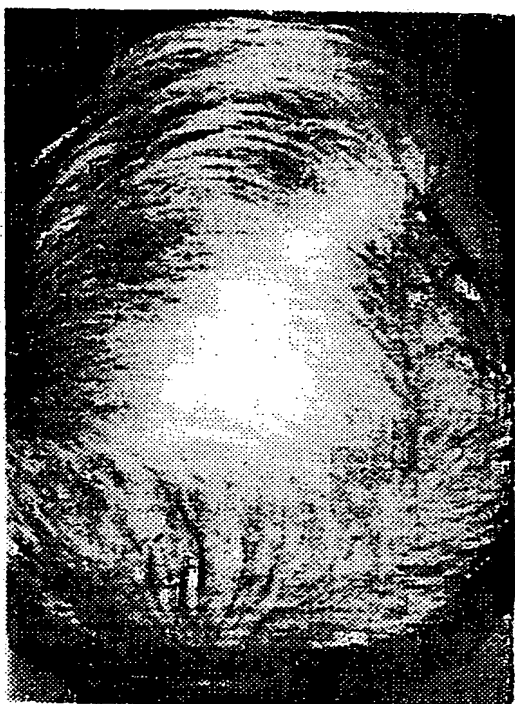


Fig 8A



Fig 8B

FIG 9

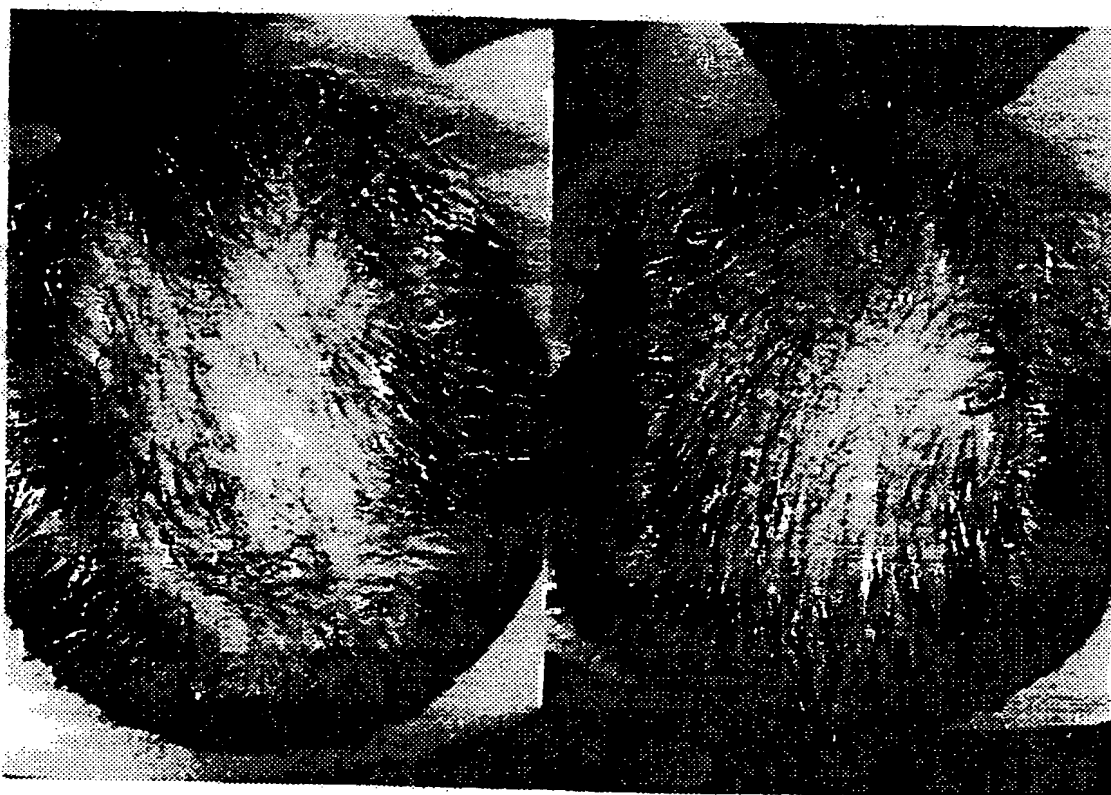


Fig 9A

Fig 9B

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/AU 99/00607

<b>A. CLASSIFICATION OF SUBJECT MATTER</b>		
Int Cl <sup>6</sup> : A61K 038/18, 19, 20, 21, 25, 30, 47, 035/78		
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b>		
Minimum documentation searched (classification system followed by classification symbols) A61K with electronic database as indicated below		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched AU:IPC as above		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) CAPLUS/PUB MED/WPAT: Hair and/or topical and/or interferon and/or interleukin and/or IGF* and/or EGF* and/or Echinacea and/or mannin and/or heteroxylan and/or arabinorhamnogalactan and/or glucan		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	Acta Derm Venereol (stockh) 1996; 76(1), pages 17-20, Hoffmann et al., "Growth Factor mRNA levels in Alopecia Areata Before and After Treatment with the Contact Allergen <u>Diphenylcyclopropenone</u> ".	1, 2, 5, 6-8, 10, 12, 13 3, 4, 9, 11
X Y	J. Am. Acad. Derm (1987), 16 (5 part (i), pages 977-983, Galbraith et al., "A Randomized Double-blind study of inosiplex (isoprinosina) therapy in Patients with Alopecia totalis".	1, 5-7, 10, 12, 13 2-4, 8, 9, 11
X Y	Brit. J. Derm. (1996), vol. 135 pages 211-217, McElwee et al., "In vivo depletion of C08T cells restores hair growth in the DEBR model for alopecia areata.	1, 5-7, 10, 12, 13 2-4, 8, 9, 11
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C <input checked="" type="checkbox"/> See patent family annex		
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## INTERNATIONAL SEARCH REPORT

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	Arch. Derm. Res. (1997) vol. 289, pages 384-388, Thein et al., "Lesional alopecia areata T lymphocytes down regulate epithelial cell proliferation.	1, 2, 5-8, 10, 12, 13 3, 4, 9, 11
X Y	Gastroent (1993) vol. 104, pages 1187-1191, Treem et al., "Ulcerative Colitis and Total Alopecia in a Mother and Son.	1, 5-7, 10, 12, 13 2-4, 8, 9, 11
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X Y	US 4839164 (Estee Lauder Inc.) 13 June 1989.	1, 5-7, 10, 12, 13 2-4, 8, 9, 11
X Y	US 5616471 (USA as rep. Dept. Health and Human Services) 1 April 1997 - in partic. examples and col. 5 line 65 - col. 6 line 5.	1, 2, 5-8, 10, 12, 13 3, 4, 9, 11
X Y	EP-A-335554 (UNILEVER PLC) 4 October 1989.	1-3, 5-10, 12, 13 4, 11
X Y	US 5599558 (Curature Technologies Inc.) 4 February 1997 -in partic. col. 4 lines 46 - col. 5 line 31.	1, 5-7, 10, 12, 13 2-4, 8, 9, 11
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X	WO 96/21463 A (Nika Health Products Ltd.) 18 July 1996 -in partic. page 5 lines 13-31 and example 2.	1-13
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X Y	Derwent Abs. Acc. No. 186-051905/08, Class B04 D21, JP-A-61005006 (Nippon Chem. Res. KK(Sank), 10 January 1986).	1, 2, 5-8, 10, 12, 13 3, 4, 9, 11



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